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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,408	08/24/2001	Roberta K. Yoshida	29479/500NSCA	5670
4743	7590	09/22/2004	EXAMINER	
MARSHALL, GERSTEIN & BORUN LLP 6300 SEARS TOWER 233 S. WACKER DRIVE CHICAGO, IL 60606			SAIDHA, TEKCHAND	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/939,408

**Applicant(s)**

YOSHIDA ET AL.

**Examiner**

Tekchand Saidha

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) 4,7-10,16,18,22,23,26,27 and 29-36 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1,2,5,11 and 12 is/are allowed.
- 6) ☒ Claim(s) 3, 6,13-15,17,19-21,24,25 and 28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### 1. ***Election***

Applicant's election of Group I, claims 1-3, 5-6, 11-15, 17, 19-21, 23-25 & 28 with traverse, filed 20 July 2004, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP §818.03(a)).

2. Claims 1-3, 5-6, 11-15, 17, 19-21, 24-25 & 28 are under consideration in this examination.

### 3. **Claims withdrawn** :

Claims 4, 7-10, 16, 18, 22-23, 26-27 & 29-36 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Please Note: Claims 22-23, using a construct (or host cell) comprising the polynucleotide of claim 4, belongs to Group II, was mistakenly grouped under Group I, is properly re-restricted under Group II and therefore withdrawn from further consideration.

### 4. ***Continuation of prior application***

Applicants' continuation data, on page 1, lack reference to the patent number. The specification must therefore be amended as follows: This application is a continuation-in-part application of U.S. patent application 09/624,693, filed July 24, 2000, now US Patent 6,355,468 and is a continuation-in-part.....

### 5. ***Priority***

Acknowledgment is made of applicants' claim for priority under 35 U.S.C. 120 or 121 to US application No. 09/624,693 filed on 24 July 2000.

### 6. ***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is

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requested in correcting any errors of which applicant may become aware in the specification.

7. ***Claim Rejections - 35 USC §112*** (first paragraph)

***Enablement***

Claims 3,14,17 & 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide [SEQ ID NO: 12], encoding a yeast phenylalanine ammonia lyase (PAL) of SEQ ID NO: 13, vector, host cell and method of making the polypeptide recombinantly, does not reasonably provide enablement for any polynucleotide encoding PAL, wherein said PAL is at least 90% identical to SEQ ID NO: 13 or any polynucleotide which is at least 80%, 90% or 95% identical to SEQ ID NO: 12 (nucleotides 37-2196). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The scope of the claims does not commensurate with the enablement provided by the disclosure with regard to the large number of polynucleotides (or nucleic acid) broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide sequence of SEQ ID NO: 12 and the encoded amino acid sequence of SEQ ID NO: 13.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's

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sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of DNA of SEQ ID NO: 12 by 5% to 20%, because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting phenylalanine ammonia lyase activity; (B) the general tolerance of phenylalanine ammonia lyase of SEQ ID NO: 12 to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any phenylalanine ammonia lyase residues with an expectation of obtaining the desired enzymatic or biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. This is further supported in the work of Seffernick et al. [J. Bacteriol. Apr. 2001, p. 2405-2410] where melamine Deaminase and Atrazine chlorohydrolase each consists of 475 amino acids, are 98% identical and are yet functionally different. Thus there is high unpredictability associated with respect to modification(s) of the sequence of SEQ ID Nos: 12 or 13 unless guidance is provided in establishing (A) – (D) as discussed above.

Thus, applicants have **not** provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of exact nature of phenylalanine ammonia lyase encoding DNA (or polynucleotide) having the desired biological characteristics, as well as vector or host cell

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constructs is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

8. ***Claim Rejections - 35 USC § 112*** (second paragraph)

Claims 6, 13-15, & 19 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6 (lines 3, 5, 9, 11, 13 & 15-22), claims 13-15 (lines 2-3), & claim 19 (line 2) recite the term 'residues' in relation to a polynucleotide sequence. The claims are indefinite because the term 'residues' is relevant in the context of an amino acid sequence, and not in context with a nucleotide sequence. The term 'nucleotides' is appropriate in context with a nucleotide sequence. Substituting 'residues' with 'nucleotides' is suggested to overcome this rejection.

9. Claim 6 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 recites 'abbreviations' B, D, H, V, Y, W, S, M, K & **T**. While the specification defines the abbreviations B, D, .. through K; T remains not defined and unclear. The claim is indefinite because these designated abbreviations are not art accepted. It is suggested to substitute the 'definition of the abbreviation(s)' for the 'abbreviation' in the claim. For example, in claim 6, lines 5-8, substitute "nucleotides 13, 34, .....and 1976 are C or G or T (or U)" for "nucleotides 13, 34, .....and 1976 are B", and so on; or other suitable amendment will overcome this rejection.

10. Claims 20-21, 24-25 & 28 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 20 & 24, line 1, recite the phrase 'A construct'. It is unclear what construct is being referred to. Is it a 'vector construct', or a 'transformed host cell construct' or some other construct. Clarification is requested.

Claims 21, 25 & 28 are included in the rejection for failing to correct the defect present in the base claim(s).

11. The following sequence search alignments are made of record but have not been used in any rejection.

Accession No. AAP80513 (PAL) and Applicants SEQ ID NO: 21 (PAL), are 89.9% identical [EP279665-A, 24 August 1988].

Accession No. AAN81116 (DNA encoding PAL) and Applicants SEQ ID NO: 20 (DNA encoding PAL), are 67.8% identical [EP279665-A, 24 August 1988].

Accession No. E01783 (DNA encoding PAL) and Applicants' SEQ ID NO: 20, are 67.8% identical [JP 1988317086-A, 29 September 1997].

12. Claims 1-2, 5 & 11-12 are allowed.

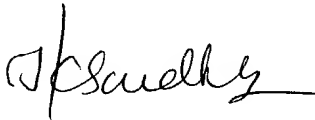
13. Claims 3, 6, 13-15, 17, 19-21, 24-25 & 28 are rejected.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on Monday-Friday, between 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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September 15, 2004